

Application No.: 10/596,103  
Amendment Submitted with RCE dated November 23, 2009  
Reply to Office Action of July 22, 2009  
Docket No.: 1848-7 PCT/US/RCE  
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### **REMARKS**

Pursuant to the submission required under 37 CFR 1.114 for a Request for Continued Examination, Applicants respectfully request entry and consideration of the Amendment and Response submitted herewith.

### **STATUS OF CLAIMS**

Claims 17-28 are pending. Please amend Claims 17-28. Support for the claim amendments can be found throughout the specification and in the claims as originally filed. No new matter has been added.

### **35 U.S.C. §112, SECOND PARAGRAPH REJECTIONS**

**Claims 17-20 and 23-26** stand rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite as detailed below.

**Claims 17 and 19-20** (from which **Claims 18-20 and 23-26** depend) recite the term “residue” which is allegedly indefinite. Applicants respectfully traverse the rejection. One of ordinary skill in the art would understand the term “residue” in the context of specific amino acid residues recited in the claims. Applicants point out that 37 CFR 1.821 incorporates by reference the World Intellectual Property Organization (WIPO) Handbook on Industrial Property Information and Documentation, Standard ST.25 (1998), including Tables 1 through 6 of Appendix 2. Notably, WIPO Standard ST.25 (1998), Appendix 2, Table 6, provides feature keys related to protein sequences and repeatedly recites the term “residue” therein to refer to amino acids and potential modifications thereto. For example, as recited therein, the key “MOD\_RES” describes “post-translational modification of a residue” and the key “MYRISTATE” describes “myristate group attached through an amide bond to the N-terminal glycine residue of the mature form of a protein or to an internal lysine residue” (see, Manual of Patent Examining Procedure, Edition 8, August 2001, Last Revision July 2008, Section 2422 “Nucleotide and/or Amino Acid Sequence Disclosures in Patent Applications,” WIPO Standard ST.25 (1998), Appendix 2, Table 6).

**Claim 17** (from which **Claims 18-20 and 23-24** depend) recite the phrase “a peptide derived from the Bbeta chain of the fibrin” which is allegedly indefinite. Applicants have amended Claim 17 so that it further recites a specific amino acid sequence that corresponds to amino acids 20-42 of the fibrin Bβ-chain.

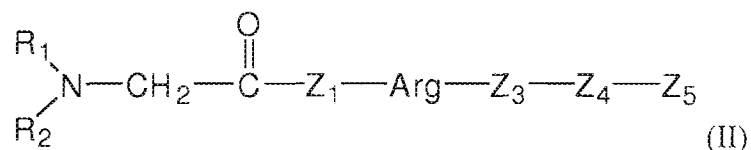
In view of the aforementioned amendment, Applicants respectfully request withdrawal of these rejections under 35 U.S.C. §112, second paragraph.

### **35 U.S.C. §112, FIRST PARAGRAPH REJECTIONS**

**Claim 17-18 and 23-24** stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement and written description. Notably, Claims 18 as well as 23-24 are dependent on independent Claim 17.

As amended, Claim 17 reads as follows:

A method for treating shock comprising administering to a subject an effective amount of a peptide of Formula II



wherein:

R<sub>1</sub> and R<sub>2</sub> being equal or different denote hydrogen, a saturated or unsaturated hydrocarbon comprising from 1 to 10 carbon atoms;

Z<sub>1</sub> denotes a histidine residue;

Arg denotes an arginine residue;

Z<sub>3</sub> denotes a proline or valine residue;

Z<sub>4</sub> denotes a leucine or valine residue; and

Z<sub>5</sub> denotes a peptide derived from the Bbeta chain of the

fibrin, which peptide has the biological property of matching the inducible VE-cadherin binding motif on the B $\beta$ -chain (i.e., B $\beta$ <sub>15-42</sub>) of human fibrin comprising:  
Asp-Lys-Lys-Arg-Glu-Glu-Ala-Pro-Ser-Leu-Arg-Pro-Ala-Pro-Pro-Pro-Ile-Ser-Gly-Gly-Gly-Tyr-Arg.

As amended, Claim 17 recites a specific amino acid sequence which Z<sub>5</sub> comprises that corresponds to amino acids 20-42 of the fibrin B $\beta$ -chain. Thus, the peptide of Formula II encompasses fibrin B $\beta$ <sub>15-42</sub> reproduced below (with amino acids 20-42 of the fibrin B $\beta$ -chain placed in bold text),

Gly-His-Arg-Pro-Leu-**Asp-Lys-Lys-Arg-Glu-Glu-Ala-Pro-Ser-Leu-Arg-Pro-Ala-Pro-Pro-Pro-Ile-Ser-Gly-Gly-Gly-Tyr-Arg**

whose activity was examined both in the treatment of mice infected with dengue virus and in the treatment of Gram-negative shock in rats, as well as a few derivatives thereof modified at the amino terminal portion of this peptide. Notably, Formula II includes the non-polar, neutral amino acid Valine at positions Z<sub>3</sub> and/or Z<sub>4</sub> in addition to the non-polar, neutral amino acids that occur in fibrin B $\beta$ <sub>15-42</sub>, namely, Proline at position Z<sub>3</sub>, Leucine at position Z<sub>4</sub>. Additionally, Formula II includes N-terminal modification whereby the terminal nitrogen of the peptide may be linked to hydrogen as occurs in fibrin B $\beta$ <sub>15-42</sub>, hydrogen and a saturated or unsaturated hydrocarbon comprising from 1 to 10 carbon atoms, or saturated or unsaturated hydrocarbons comprising from 1 to 10 carbon atoms.

In support of the patentability of Claims 17-18 and 23-24, Applicants provide copies of U.S. Patent 7,271,144 (**Exhibit A**) and U.S. Patent 7,494,973 (**Exhibit B**). Both of these patents include method claims using a peptide corresponding to fibrin B $\beta$ <sub>15-42</sub> with N-terminal modifications as claimed in the present invention. Additionally, Applicants provide a copy of

the corresponding European patent EP 1 691 827 (**Exhibit C**) issued on September 19, 2008. Notably, Claim 1 of EP 1 691 827 (recited in English at page 12) includes these same N-terminal modifications as well as the conservative amino acid substitutions at positions Z<sub>3</sub> and Z<sub>4</sub> discussed above in Claim 17 of the present invention. Likewise, Claim 2 of EP 1 691 827 (which depends on Claim 1), includes the same N-terminal modifications found in Claim 18 of the presently claimed invention. Applicants contend that the genus of the presently claimed invention meets both the enablement and written description requirements as evidenced by the aforementioned patents.

In view of the aforementioned amendments and arguments, Applicants respectfully request withdrawal of these rejections under 35 U.S.C. §112, first paragraph rejections of Claims 17-18 and 23-24.

### **35 U.S.C. §102 REJECTIONS**

**Claims 17-18** stand rejected under 35 U.S.C. §102(a) and 35 U.S.C. §102(e) as allegedly being anticipated by **Petzelbauer** (US 2004/0192596). Notably, U.S.S.N. 10/459,030 (granted as U.S. Patent No. 7,271,144 on September 18, 2007) published as US 2004/0192596 on September 30, 2004 and lists Peter Petzelbauer as the sole inventor. US 2004/0192596 paragraph [0001] recites the following:

The present application is a continuation of **International Patent Application No. PCT/AT01/00387, filed Dec. 7, 2001, published in German** on Jun. 20, 2002 as International Patent Publication No. WO02/248180, which claims priority to Austrian Application No. AT A 2063/2000, filed Dec. 12, 2000, all of which are incorporated in their entireties herein.

Emphasis added. As International Patent Application PCT/AT01/00387 upon which U.S.S.N. 10/459,030 is based was not published in English, publication US 2004/0192596 is effective as a 35 U.S.C. §102(a) prior art reference only as of its publication date (i.e., September 30, 2004) and has no 35 U.S.C. §102(e) date. Thus, this 35 U.S.C. §102(e) rejection is improper.

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Additionally, the present application was filed on May 30, 2006, but claims priority to June 24, 2004. As the effective filing date of the present application is June 24, 2004 and the effective 35 U.S.C. §102(a) date of US 2004/0192596 is September 30, 2004, US 2004/0192596 is not applicable as prior art under 35 U.S.C. §102(a).

**Claims 17-18** stand rejected under 35 U.S.C. §102(a) and 35 U.S.C. §102(e) as allegedly being anticipated by **Petzelbauer** (US 2007/0037749). Notably, U.S.S.N. 11/542,050 (granted as U.S. Patent No. 7,494,973 on February 24, 2009) published as US 2007/037749 on February 15, 2007 and lists Peter Petzelbauer as the sole inventor. US 2007/0037749 paragraph [0001] recites the following:

The present application is a divisional of U.S. patent application Ser. No. 10/459,030, filed Jun. 11, 2003, which is a continuation of **International Patent Application No. PCT/AT01/00387, filed Dec. 7, 2001, published in German** on Jun. 20, 2002 as International Patent Publication No. WO02/248180, which claims priority to Austrian Application No. AT A 2063/2000, filed Dec. 12, 2000, all of which are incorporated in their entireties herein.

Emphasis added. As International Patent Application PCT/AT01/00387 upon which U.S.S.N. 11/542,050 is based was not published in English, publication US 2007/0037749 is effective only as of its publication date (i.e., February 15, 2007). Thus, this 35 U.S.C. §102(e) rejection is improper. Additionally, the present application was filed on May 30, 2006, but claims priority to June 24, 2004. As the effective filing date of the present application is June 24, 2004 and the effective date of US 2007/0037749 is February 15, 2007, US 2007/0037749 is not applicable as prior art under 35 U.S.C. §102(a).

As none of the aforementioned documents can anticipate the presently claimed invention under either 35 U.S.C. §102(a) and §102(e), Applicants respectfully request withdrawal of these rejections under 35 U.S.C. §102(a) and §102(e) of Claims 17-18.

### **DOUBLE PATENTING REJECTIONS**

**Claims 17-28** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-4 of U.S. Patent No. 7,271,144.

**Claims 17-28** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-4 of copending Application No. 11/899,611.

**Claims 17-28** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 6-7 of copending Application No. 12/121,533.

**Claims 17-28** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 6-7 of copending Application No. 12/121,544.

**Claims 17-28** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-2 and 4-5 of copending Application No. 12/158,670.

**Claims 17-28** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-3 of U.S. Patent No. 7,494,973.

Upon indication of allowable subject matter, Applicants will consider the need to file one or more terminal disclaimers to obviate the concerns of these nonstatutory obviousness-type double

patenting rejections. Applicants request an *Ex parte Quayle* action to address these matters once prosecution on the merits is closed.

### **OBJECTIONS**

**Claims 19-22** are objected to for lacking sequence identifiers for the peptide sequences cited therein.

**Claims 19-20** are objected to for incorrectly spelling the term “leucine.” The claims have been amended accordingly to correct this spelling error.

**Claims 23-28** are objected to for verbosity with regard to the phrase “wherein the shock is associated with one or more out of the group.” This phrase has been amended to “wherein the shock is associated with one or more from the group.”

**Claims 23-28** are objected to for incorrectly spelling the term “infectious.” The claims have been amended accordingly to correct this spelling error.

**Claims 23-28** are objected to for inconsistency with regard to spelling the term “hemorrhagic.” The claims have been amended accordingly to correct this spelling error.

In view of the aforementioned amendments, Applicants believe these objections no longer applicable.

### **AMENDMENTS TO THE SPECIFICATION**

The specification has been amended to provide a cross-reference to reflect that the present application is a National Stage Application under §371 of International Application No. PCT/AT2005/000228, filed May 30, 2006, which claims priority to Austrian applications A 1087/2004 filed June 24, 2004 and A 40/2005 filed January 13, 2005.

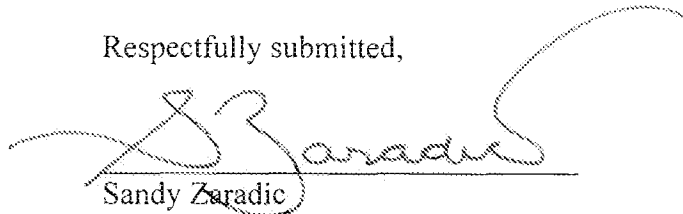
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**CONCLUSION**

Applicants believe Claims 17-28 are in condition for allowance and respectfully request the same.

If there are any questions or if additional information is required, the Examiner is respectfully requested to contact Applicants' attorney at the number listed below.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read 'Sandy Zaradic', is written over a horizontal line. The signature is stylized with a large, sweeping initial 'S' and a long, curved flourish extending to the right.

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